

CANCELLED

per A

Sub B4

WHAT WE CLAIM IS:

1. A DNA sequence selected from the group consisting of the DNA inserts of G-pBR322(Pst)/HFIF1, G-pBR322(Pst)/HFIF3, G-pBR322(Pst)/HFIF-6, G-pBR322(Pst)/HFIF7, DNA sequences which hybridize to any of the foregoing DNA inserts and DNA sequences, from whatever source obtained, including natural, synthetic or semi-synthetic sources, related by mutation, including single or multiple, base substitutions, deletions, insertions and inversions to any of the foregoing DNA sequences or inserts.

2. A DNA sequence according to claim 1 wherein said DNA sequence which hybridizes to said DNA insert is selected from the group consisting of the DNA inserts of G-pPLA-HFIF-67-12, G-pPLA-HFIF-67-12A19, G-pPLC-HFIF-67-8, DNA sequences which hybridize to any of the foregoing DNA inserts, DNA sequences, from whatever source obtained, including natural, synthetic or semi-synthetic sources, related by mutation, including single or multiple, base substitutions, deletions, insertions and inversions to any of the foregoing DNA sequences or inserts, and DNA sequences comprising sequences of codons which on expression code for a polypeptide displaying similar immunological or biological activity to a polypeptide coded for on expression of the codons of any of the foregoing DNA sequences and inserts.

3. A DNA sequence according to claim 1 or 2 wherein said DNA sequence which hybridizes to said DNA insert is selected from the group consisting of G-pPLA-HFIF-67-12A279T, G-pPLA-HFIF-67-12A218M1, G-pPLA-HFIF-67-12AM1, G-pPLA-HFIF-67-12A19 BX-2, DNA sequences which hybridize to any of the foregoing DNA sequences, DNA sequences, from whatever source obtained, including natural, synthetic, or semi-synthetic sources, related by mutation, including single or multiple, base substitutions, deletions, insertions and inversions, to any of the foregoing DNA sequences and DNA sequences comprising sequences of codons which on expression code for a polypeptide

CANCELLED

per A

CANCELLED

per A

similar in immunological or biological activity to a polypeptide coded for on expression of any of the foregoing DNA sequences.

4. A DNA sequence according to anyone of claims 1 to 3 wherein said DNA sequence which hybridizes to said DNA insert is the DNA insert of p[325]-GHFIF-4, DNA sequences which hybridize to the foregoing DNA sequence, DNA sequences, from whatever source obtained, including natural, synthetic, or semi-synthetic sources, related by mutation, including single or multiple, base substitutions, deletions, insertions and inversions, to the foregoing DNA sequences and DNA sequence comprising sequences of codons which on expression code for a polypeptide similar in immunological or biological activity to a polypeptide coded for on expression of the foregoing DNA sequence.

5. A DNA sequence according to any one of claims 2 to 4 characterized in that it is selected from the group consisting of DNA sequences of the formula: ATGACCAACAAG TGTCTCCTCCAAATTGCTCTCCTGTGTCTTCTCCACTACAGCTCTTTCCATGAGC TACAACCTTGCTTGGATTCTTACAAAGAAGCAGCAATTTTCAGTGTGAGAAGCTCCTG TGGCAATTGAATGGGAGGCTTGAATACTGCCTCAAGACAGGATGAACCTTTGACATC CCTGAGGAGATTAAAGCAGCTGCAGCAGTTCCAGAAGGAGGACGCCGATTGACCATC TATGAGATGCTCCAGAACATCTTTGCTATTTTCAGACAAGATTCTAGCACTGGC TGGAAATGAGACTATTGTTGAGAACCTCCTGGCTAATGTCTATCATCAGATAAACCAT CTGAAGACAGTCTGGAAGAAAACCTGGAGAAAGAAGATTTACCAGGGGAAAACCTC ATGAGCAGTCTGCACCTGAAAAGATATTATGGGAGGATTCTGCATTACCTGAAGGCC AAGGAGTACAGTCACTGTGCCTGGACCATAGTCAGAGTGGAAATCCTAAGGAACCTTT TACTTCATTAACAGACTTACAGGTTACCTCCGAAAC, ATGAGCTACAACTTGCTT GGATTCTTACAAAGAAGCAGCAATTTTCAGTGTGAGAAGCTCCTGTGGCAATTGAAT GGGAGGCTTGAATACTGCCTCAAGACAGGATGAACCTTTGACATCCCTGAGGAGATT AAGCAGCTGCAGCAGTTCCAGAAGGAGGACGCCGATTGACCATCTATGAGATGCTC CAGAACATCTTTGCTATTTTCAGACAAGATTCTAGCACTGGCTGGAATGAGACT ATTGTTGAGAACCTCCTGGCTAATGTCTATCATCAGATAAACCATCTGAAGACAGTC CTGGAAGAAAACCTGGAGAAAGAAGATTTACCAGGGGAAAACCTCATGAGCAGTCTG CACCTGAAAAGATATTATGGGAGGATTCTGCATTACCTGAAGGCCAAGGAGTACAGT CACTGTGCCTGGACCATAGTCAGAGTGGAAATCCTAAGGAACCTTTTACTTCATTAAC AGACTTACAGGTTACCTCCGAAAC and derivatives thereof, said

APPROVED

per A

APPROVED

per A

29/3/89

29/3/89

fragments and derivatives coding for polypeptides displaying an immunological or biological activity of IFN- β .

(6) A recombinant DNA molecule characterized by a DNA sequence according to any one of the preceding claims.

(7) The recombinant DNA molecule according to claim 6, characterized in that said DNA sequence is operatively linked to an expression control sequence.

(8) The recombinant DNA molecule according to claim 7, characterized in that said expression control sequence is selected from the group consisting of a lac system, a β -lac system, a trp system, major operator and promotor regions of phage λ , the control region of fd coat protein, and other sequences which control the expression of genes of prokaryotic or eukaryotic cells and their viruses.

(9) The recombinant DNA molecule according to claim 7 or 8 selected from the group consisting of G-pPLa-HFIF-67-12, G-pPLa-HFIF-67-12 Δ 19, and G-pPLa-HFIF-67-8.

(10) The recombinant DNA molecule according to claim 7 or 8 characterized in that it is selected from the group consisting of G-pPLa-HFIF-67-12 Δ 279T, 6-pPLa-HFIF-67-12 Δ 218M1, 6-pPLa-HFIF-67-12 Δ M1, and G-pPLa-HFIF-67-12 Δ 19 BX-2.

(11) A host transformed with at least one recombinant DNA molecule, said recombinant DNA molecule being selected from the group consisting of recombinant DNA molecules according to any one of claims 6 to 10.

(12) The host of claim 11 selected from the group consisting of strains of E. coli, Pseudomonas, Bacillus subtilis, Bacillus stearothermophilus, other bacilli, yeasts, other fungi, mouse or other animal or plant hosts and human tissue cells.

(13) The transformed host according to claim 11 or 12 selected from the group consisting of E. coli HB101 (G-pBR322(Pst)/HFIF1), E. coli HB101 (G-pBR322(Pst)/HFIF3), E. coli HB101 (G-pBR322(Pst)/HFIF6) and E. coli HB101 (G-pBR322(Pst)/HFIF7).

CANCELLED

per A

5

CANCELLED

per A

CANCELLED

per A

10

15

per A

Subt B5

20

CANCELLED

per A

25

per A

CANCELLED

per A

30

Subt B6

35

CANCELLED
per A ^{subt} B6

AMENDED 1635
per A 243

AMENDED
per A 160 11v.5

AMENDED per A

CANCELLED
per A

37 CFR 1.643

14. The transformed host according to claim 11 or 12 selected from the group consisting of E.coli M5219 (G-pPLa-HFIF-67-12), E.coli K12ΔHI (G-pPLa-HFIF-67-12), E.coli M5219 (G-pPLa-HFIF-67-12Δ19), E.coli M5219 (G-pPLC-HFIF-67-8) and E.coli K12ΔHI (G-pPLa-HFIF-67-8)

15. The transformed host according to claim 11 and 12 characterized in that it is selected from the group consisting of E.coli M5219 (G-pPLa-HFIF-67-12Δ279T), E.coli M5219 (pPLa-HFIF-67-12Δ218M1), E.coli M5219 (pPLa-HFIF-67-12ΔM1), E.coli K12ΔHI (pPLa-HFIF-67-12Δ19 BX-2).

16. A polypeptide or fragments and derivatives thereof (displaying an immunological or biological activity of human fibroblast interferon) produced by the transformed host according to any one of claims 11 to 15.

17. A polypeptide characterized in that it is coded for by a DNA sequence according to any one of claims 1 to 5.

18. A polypeptide or fragments and derivatives thereof according to claim 16 or 17 and being IFN-β.

19. A polypeptide or fragments and derivatives thereof according to any one of claims 16 to 18 characterized in that it is selected from the group consisting of polypeptides of the formula: Met-Thr-Asn-Lys-Cys-Leu-Leu-Gln-Ile-Ala-Leu-Leu-Leu-Cys-Phe-Ser-Thr-Thr-Ala-Leu-Ser-Met-Ser-Tyr-Asn-Leu-Leu-Gly-Phe-Leu-Gln-Arg-Ser-Ser-Asn-Phe-Gln-Cys-Gln-Lys-Leu-Leu-Trp-Gln-Leu-Asn-Gly-Arg-Leu-Glu-Tyr-Cys-Leu-Lys-Asp-Arg-Met-Asn-Phe-Asp-Ile-Pro-Glu-Glu-Ile-Lys-Gln-Leu-Gln-Gln-Phe-Gln-Lys-Glu-Asp-Ala-Ala-Leu-Thr-Ile-Tyr-Glu-Met-Leu-Gln-Asn-Ile-Phe-Ala-Ile-Phe-Arg-Gln-Asp-Ser-Ser-Ser-Thr-Gly-Trp-Asn-Glu-Thr-Ile-Val-Glu-Asn-Leu-Leu-Ala-Asn-Val-Tyr-His-Gln-Ile-Asn-His-Leu-Lys-Thr-Val-Leu-Glu-Glu-Lys-Leu-Glu-Lys-Glu-Asp-Phe-Thr-Arg-Gly-Lys-Leu-Met-Ser-Ser-Leu-His-Leu-Lys-Arg-Tyr-Tyr-Gly-Arg-Ile-Leu-His-Tyr-Leu-Lys-Ala-Lys-Glu-Tyr-Ser-His-Cys-Ala-Trp-Thr-Ile-Val-Arg-Val-Glu-Ile-Leu-Arg-Asn-Phe-Tyr-Phe-Ile-Asn-Arg-Leu-Thr-Gly-Tyr-Leu-Arg-Asn, Met-Ser-

CANCELLED
per A

37 CFR 1.663

CANCELLED
per A (3)
68

CANCELLED
per A

per A

per A
37 CFR 1.663

5 Tyr-Asn-Leu-Leu-Gly-Phe-Leu-Gln-Arg-Ser-Ser-Asn-Phe-Gln-
Cys-Gln-Lys-Leu-Leu-Trp-Gln-Leu-Asn-Gly-Arg-Leu-Glu-Tyr-
Cys-Leu-Lys-Asp-Arg-Met-Asn-Phe-Asp-Ile-Pro-Glu-Glu-Ile-
Lys-Gln-Leu-Gln-Gln-Phe-Gln-Lys-Glu-Asp-Ala-Ala-Leu-Thr-
10 Ile-Tyr-Glu-Met-Leu-Gln-Asn-Ile-Phe-Ala-Ile-Phe-Arg-Gln-
Asp-Ser-Ser-Ser-Thr-Gly-Trp-Asn-Glu-Thr-Ile-Val-Glu-Asn-
Leu-Leu-Ala-Asn-Val-Tyr-His-Gln-Ile-Asn-His-Leu-Lys-Thr-
Val-Leu-Glu-Glu-Lys-Leu-Glu-Lys-Glu-Asp-Phe-Thr-Arg-Gly-
Lys-Leu-Met-Ser-Ser-Leu-His-Leu-Lys-Arg-Tyr-Tyr-Gly-Arg-
15 Ile-Leu-His-Tyr-Leu-Lys-Ala-Lys-Glu-Tyr-Ser-His-Cys-Ala-
Trp-Thr-Ile-Val-Arg-Val-Glu-Ile-Leu-Arg-Asn-Phe-Tyr-Phe-
Ile-Asn-Arg-Leu-Thr-Gly-Tyr-Leu-Arg-Asn, and polypeptides
from whatever source obtained related to any of the
foregoing polypeptides by mutation, including single or
multiple, base substitutions, deletions, insertions and
inversions, to any of the DNA sequences which code for
them.

20. A method for producing a recombinant DNA
molecule characterized by the step of introducing into a
cloning vehicle a DNA sequence according to any one of
claims 1-5.

21. The method according to claim 20 character-
ized by the additional step of introducing into said cloning
vehicle an expression control sequence according to
claim 8, said expression control sequence being introduced
into said cloning vehicle so as to control and to regulate
the expression of said DNA sequence.

22. A method for transforming a host characterized
by the step of introducing into a host a recombinant DNA
molecule according to any one of claims 6 to 10.

23. A method for producing a polypeptide
displaying an immunological or biological activity of
human fibroblast interferon, characterized by the steps
of transforming an appropriate host with a recombinant DNA
molecule according to any one of claims 8 to 10; culturing
said host, and collecting said polypeptide.

CANCELLED

per A

per A
37 CFR 1.663 5

per A Sub B7

CANCELLED

per A

CANCELLED
per A
37 CFR 1.663
424

NE
2/13/81

CANCELLED
per A
35
37 CFR 1.663

24. The method according to claim 23, characterized in that the host is selected from the group consisting of strains of E. coli, Pseudomonas, Bacillus subtilis, Bacillus stearothermophilus, other bacilli, yeasts, fungi, animal or plant hosts, and human tissue cells.

25. A method for producing a polypeptide displaying an immunological or biological activity of human fibroblast interferon characterized by the steps of culturing a host transformed by a recombinant DNA molecule according to any one of claims 8 to 10 and collecting said polypeptide.

26. A process for selecting a DNA sequence coding for a polypeptide displaying an immunological or biological activity of HuIFN- β from a group of DNA sequences characterized by the step of determining which of said DNA sequences hybridizes to a DNA sequence according to any one of claims 1-5.

27. The process of claim 26 wherein said DNA sequence screened is selected from the group consisting of DNA sequences from natural sources, synthetic DNA sequences, DNA sequences from recombinant DNA molecules and DNA sequences which are a combination of any of the foregoing DNA sequences.

28. A composition for treating human viruses or treating human cancers or tumors characterized by at least one polypeptide selected from the group consisting of the polypeptides, according to any one of claims 16 to 18.

~~29. A composition for treating bovine viral infections characterized by at least one polypeptide selected from the group consisting of polypeptides, according to any one of claims 16 to 18.~~

~~21.20. A method for treating human viruses or treating human cancers or tumors characterized by the step of administering to said humans in a pharmaceutically acceptable manner an effective amount of a composition according to claim 28.~~

WE 29/3/84

~~31. A method for treating bovine viral infections characterized by the step of administering to said animals in a pharmaceutically acceptable manner an effective amount of a composition according to claim 29.~~

WE 29/3/84

CANCELLED
per A

37 CR 1.663

~~30. A polypeptide or fragments and derivatives thereof coded for by a DNA sequence that does not hybridize to a DNA sequence according to any one of claims 1 to 5 and which displays an immunological activity of IFN- β , which activity is destroyed by antisera to authentic IFN- β .~~

add C'

CANCELLED claims 1-15, 19-30 per A

ADDED CLAIMS 31-37 per A

add B⁴